IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TENNESSEE
WESTERN DIVISION

FREDDIE JONES, LUKE JONES, TRENNA JONES, RALPH JONES, LAVON JONES, and JIMMY FREEMAN, as Surviving Children of ELNORA JONES, Deceased, Plaintiffs, vs. ABBOTT LABORATORIES, Defendant.	)	Case No. 2:07-cv-02120-BBD-tmp JURY DEMAND

ABBOTT LABORATORIES' REPLY MEMORANDUM IN SUPPORT OF ITS MOTION FOR A PROTECTIVE ORDER QUASHING PLAINTIFFS' REQUEST FOR ABBOTT'S ADVERSE EVENT REPORTS DATABASE

Defendant Abbott Laboratories ("Abbott"), by and through its undersigned counsel, respectfully submits its Reply Memorandum in Support of Its Motion for a Protective Order Quashing Plaintiffs' Request for Abbott's Adverse Event Reports Database, and in support states as follows:

I. Plaintiffs Have Failed To Demonstrate A Particularized Need For The Production Of Abbott's AEGIS Database Because Their Proposed PRR Analysis Is Irrelevant.

Plaintiffs do not dispute that because Abbott has already produced the adverse event reports for Humira involving cancers in electronically text-searchable PDF format, the Rules of this Court require them to "demonstrate a particularized need" for production of that same information in its native format. L.R. 26.1(e)(6); *see also* Dkt. # 150 at 8-10. The sole "particularized need" that Plaintiffs identified at the June 13, 2011 hearing was that the database

is necessary to conduct proportional reporting rate ("PRR") analyses of Humira adverse event reports. As described by Plaintiffs, they plan to use PRR analyses to compare the reporting ratios of one adverse event coincident with the use of Humira to another—e.g., lymphomas and infections. Plaintiffs, however, misunderstand the function and purpose of PRR analyses. PRR analysis is not intended to compare reporting ratios of different adverse events associated with the same drug. Instead, it compares the frequency of spontaneous reports of a specific adverse event for a particular drug with the frequency of reports of that same adverse event for ***other*** drugs.[1] Moreover, Plaintiffs have presented to the Court no case law, FDA guidance, or any other authority whatsoever (and Abbott has found none) to support Plaintiffs' argument that their "version" of PRR analysis is an accepted means of signal detection in pharmacovigilance planning.

Even if Plaintiffs intend to conduct a traditional PRR analysis and compare the reporting ratio of cancers for Humira with the reporting ratio of cancers for other drugs, the calculations produced by such analysis would be irrelevant to any claim or defense in this case—particularly Plaintiffs' causation inquiry. The FDA has specifically determined that "data mining techniques" such as PRR analysis are "not a tool for establishing causal attributions between products and adverse events." FDA Final Guidance, "Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment" (March 2005), Sec. IV.E, at *7 (attached hereto as Ex. C). The FDA has also acknowledged that techniques like PRR analysis "are still in development and their usefulness for identifying safety signals is being evaluated[,]" that they "do[] not quantify the magnitude of risk, and [that] caution should be exercised when comparing drugs." FDA

[1] *See generally* S. J. W. Evans, et al., "Proportional Reporting Ratios: the Uses of Epidemiological Methods for Signal Generation [abstract]," Pharmacoepidemiology and Drug Safety 7:S79-S215 (1998) (attached hereto as Ex. A); S. J. W. Evans, et al., "Use of Proportional Reporting Ratios (PRRs) for Signal Generation From Spontaneous Adverse Drug Reaction Reports," Pharmacoepidemiology and Drug Safety 10:483-486 (2001) (attached hereto as Ex. B).

Final Guidance, "E2E Pharmacovigilance Planning" (April 2005), Sec. IV.1, at *8 (attached hereto as Ex. D).[2]

There is no dispute in the pharmacovigilance literature that PRR analysis is not a means of demonstrating causation; instead, it is simply one technique for a drug manufacturer "to detect potential signals for further evaluation." *See id.* Moreover, several commentators have criticized the use of PRR analysis even for this extremely limited purpose, because the analysis is based entirely on adverse event reports—widely recognized as an incomplete and biased data source. *See, e.g.*, Brian L. Strom, "Potential for Conflict of Interest in the Evaluation of Suspected Adverse Drug Reactions: A Counterpoint," JAMA, Vol. 292, No. 21, Dec. 2004, at 2644 (criticizing analyses like PRR as "formal statistical analyses of poor, incomplete, and biased data" and noting that "[n]o matter how sophisticated, analyses of such data can readily be misleading.") (attached hereto as Ex. E).

And as this Court has already noted, all other courts that have addressed the issue have specifically rejected use of PRR analyses in product liability litigation, finding that it "does not speak to the issue of causation" and that "proportional reporting rate analyses are incomplete and often misleading[.]" *In re Meridia Prods. Liab. Litig.*, 328 F. Supp. 2d 791, 807 (N.D. Ohio 2004); *see also id.* at 808 (finding that "this determination is consistent with other courts' conclusions regarding proportional reporting rate analyses" and collecting cases). Plaintiffs' Response fails to address *In re Meridia* and does not explain how their proposed PRR analysis would be any more relevant in this case. Because the results of any PRR analysis sought by Plaintiffs would be of questionable relevance at best, the enormous burden of producing the database outweighs Plaintiffs' purported "particularized need" for the data.

[2] *See also id.* ("Results of data mining should be interpreted with the knowledge of the weaknesses of the spontaneous reporting system and, more specifically, the large differences in the ADR reporting rate among different drugs and the many potential biases inherent in spontaneous reporting.").

II. Even If Plaintiffs' Proposed PRR Analysis Were Relevant, Plaintiffs Have Not Shown That They Need Data From Abbott's AEGIS Database To Conduct It.

Even if Plaintiffs' proposed PRR analysis had any relevance to their claims, Plaintiffs have not demonstrated why they need Abbott's entire AEGIS database to conduct their analysis. First, in order to compare the reporting ratios of Humira to other drugs, Plaintiffs require access to the AERs of these other drugs, which are not contained in Abbott's database. Presumably, Plaintiffs' experts will obtain this data from the FDA's Adverse Event Reporting System ("AERS"), which collects adverse events reports for all drugs from all manufacturers and other sources. Because the FDA database contains the AERs for Humira and all other drugs, Plaintiffs simply have no "particularized need" for Abbott's AEGIS database. Second, the standard PRR equation requires only the cumulative number of adverse event reports of interest (here, cancers) and the total number of all adverse event reports, and does not require the number of other adverse event reports (for example, infections or neurological disorders) or any other information from the AEGIS database (for example, narrative fields).[3] In short, the production of the entire AEGIS database is not required for Plaintiffs to conduct a PRR analysis. Plaintiffs have made no argument and provided this Court with no reason why Abbott should undertake the burden and expense of producing its database in native format, given that PRR analysis—Plaintiffs' ***only*** claimed reason for why they need the database—can be performed by using other readily accessible data.

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[3] The standard PRR equation is $a/(a + b)$ divided by $c/(c + d)$, with the variables defined as follows:

	Reaction(s) of interest	All other reactions
Drug of interest	*A*	*b*
All other drugs in the database	*C*	*d*

See, e.g., Nicholas Moore, et al., "Biases Affecting the Proportional Reporting Ratio (PRR) in Spontaneous Reports Pharmacovigilance Databases: the Example of Sertindole," Pharmacoepidemiology and Drug Safety 12:271-281 (2003), at 272 (attached hereto as Ex. F).

III. Plaintiffs Ignore The Authorities Cited By Abbott And Rely Exclusively On Unreported Orders That Have Little To No Persuasive Force.

Plaintiffs do not even attempt to rebut the many authorities Abbott cited in its opening brief that establish that Plaintiffs are not entitled to the database on the grounds of irrelevance, cumulativeness, and burden. (*See* Dkt. # 150.) Instead, Plaintiffs rely exclusively on two ***unreported*** orders from foreign jurisdictions—orders that include virtually no analysis of any of the issues raised in Abbott's brief and, between the two of them, cite to just one published decision. These orders have little to no persuasive force.

In addition, the orders cited by Plaintiffs are not apposite here. Plaintiffs in *In re Neurontin* argued that the databases were relevant to their claim that defendants "market[ed] their drug Neurontin for . . . 'off-label' uses" for which they "had reason to know it was not safe." (*See* Resp., Dkt. #153, Ex. B, at 1.) The court agreed, finding that adverse event reports may be relevant to determine the extent of off-label use and defendants' awareness of it. (*See id.* at 2.) Here, however, Plaintiffs have asserted no such comparable need for Abbott's database.[4] And as Abbott has already explained, even the significant burden of producing a much smaller database in the Depakote litigation in *Rix v. Sanchez* cannot be compared to the burden of having to produce the entire Humira database—which contains over five times as many adverse event reports. (*See* Dkt. #150, at 7-8; 16-17). Unlike the *In re Meridia* court's careful articulation why a PRR analysis is irrelevant, the *Rix* court does not even discuss the issue or otherwise explain the relevance of the database. Discovery, while broad, is still closely tethered to concepts of relevance. *See* Fed. R. Civ. P. 26(b)(1); *Allen v. Howmedica Leibinger, GmhH*, 190 F.R.D. 518, 522 (W.D. Tenn. 1999) ("The party seeking discovery must be able to 'articulate the possible

[4] The *In re Neurontin* court also rejected the defendant's burden arguments because they were "conclusory." *See* Resp., Dkt. #153, Ex. B, at 3. Here, by contrast, Abbott has supported its burden arguments with a detailed declaration, which will be supplemented with live testimony at the June 23rd hearing.

linkage between the discovery sought and admissible evidence.'") (citation omitted). Moreover, neither of the orders cited by Plaintiffs address the situation here, where Abbott has already produced the AER data in the format requested by Plaintiffs' original counsel.

IV. Plaintiffs' Technical Expert Should Not Be Permitted To Participate In The June 23, 2011 Hearing Without Prior Disclosure of His Testimony.

Finally, Abbott objects to Plaintiffs' last-minute tendering of Keith Altman, Plaintiffs' "technical expert" (Resp., Dkt. #153 at 4), as a witness at the upcoming June 23, 2011 hearing without prior disclosure of his testimony. In support of its motion for a protective order, Abbott submitted a declaration from its employee Jody Trieloff that provides detailed factual support for its argument that the enormous burden of producing the AEGIS database outweighs the questionable relevance of the information. (Dkt. #150, Ex. B.) Rather than respond with their own declaration, Plaintiffs advised Abbott on June 21, 2011—***two days*** before the hearing—that they intend to present Mr. Altman as a witness. Since then, Plaintiffs have provided no information whatsoever as to Mr. Altman's qualifications, formal training, or experience, or what his proposed testimony will be. Plaintiffs' efforts to inject new issues into a fully-briefed motion at the eleventh hour should be denied, and they should not be permitted to tender Mr. Altman at the June 23, 2011 hearing.

CONCLUSION

For the foregoing reasons, Abbott respectfully requests that this Court grant its motion for a protective order and quash Plaintiffs' request for production of the AEGIS database for Humira.

Date: June 22, 2011

Respectfully submitted,

s/ Jill M. Steinberg

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that on this 22nd day of June, 2011, a copy of the foregoing was served on the parties listed below via operation of the electronic filing system of the United States District Court for the Western District of Tennessee:

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